

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) ~~An isolated mutein polypeptide selected from muteins of the bilin-binding protein of *Pieris brassicae*, characterized in that it~~ wherein said mutein

(a) is able to bind digoxigenin or digoxigenin conjugates,

(b) does not bind ouabain, testosterone and 4-aminofluorescein

and,

(c) has an amino substitution at ~~at least one~~ or more of the sequence positions 28, 31, 34, 35, 36, 37, 58, 60, 69, 88, 90, 95, 97, 114, 116, 125, and 127 of the wild type bilin binding protein (SEQ ID NO: 28).

2. (Currently Amended) The ~~mutein polypeptide~~ according to claim 1, ~~characterized in that the dissociation constant of the~~ wherein a complex formed between the mutein of the bilin binding protein and with digoxigenin is has a dissociation constant of 100 nM or less.

3. (Currently Amended) The ~~mutein polypeptide~~ according to claim 1, ~~characterized in that it~~ wherein said mutein carries, in comparison with the wild type bilin-binding protein (SEQ ID NO: 28), at least one of the amino acid substitutions selected from the group consisting of Glu(28)- > Gln, Lys(31)- > Ala, Asn(34)- > Asp, Ser(35)- > His, Val(36)- > Ile, Glu(37)- > Thr, Asn(58)- > Arg, His(60)- > Ser, Ile(69)- > Ser, Leu(88)-> Tyr, Tyr(90)-> Ile, Lys(95)-> Gln, Asn(97)-> Gly, Tyr(114)-> Phe, Lys(116)-> Ser, Gln(125)- >Met, and Phe(127)-> Leu.

4. (Currently Amended) The ~~mutein polypeptide~~ according to claim 3, ~~characterized in that it~~ wherein said mutein has the amino acid sequence depicted as SEQ ID NO: ~~23~~45.

5. (Currently Amended) The ~~mutein polypeptide as claimed in~~ of claim 1,

~~characterized in that it~~ wherein said mutein

carries at least one label group, selected from the group consisting of enzymatic label, radioactive label, fluorescent label, chromophoric label, ~~(bio)~~ luminescent label, ~~or~~ and label containing haptens, biotin, metal complexes, metals, or colloidal gold.

6. (Currently Amended) A fusion proteins comprising the mutein of polypeptides according to claim 1, wherein a fusion partner of said fusion protein is at least one member selected from the group consisting of ~~characterized in that~~ an enzyme, ~~another~~ a protein, ~~or~~ a protein domain, a signal sequence and ~~/or~~ an affinity peptide and wherein the fusion partner is fused to the amino terminus of the mutein polypeptide in an operable manner.

7. (Currently Amended) A fusion proteins comprising the mutein of polypeptides according to claim 1, wherein a fusion partner of said fusion protein is at least one member selected from the group consisting of ~~characterized in that~~ an enzyme, ~~another~~ a protein, ~~or~~ a protein domain, a targeting sequence and ~~/or~~ an affinity peptide, wherein said targeting sequence allows the transport of the fusion protein into a specific cell, and wherein the fusion partner is fused to the carboxy terminus of the mutein polypeptide in an operable manner.

8. (Withdrawn) A nucleic acid, characterized in that it comprises a sequence coding for a mutein or a fusion protein of a mutein of the bilin-binding protein according to claim 1.

9. (Withdrawn) The nucleic acid according to claim 8, characterized in that it comprises the nucleotide sequence according to SEQ ID NO:15 or another nucleotide encoding the polypeptide according to SEQ ID NO:15.

10. (Withdrawn) A method for producing digoxigenin-binding muteins of the bilin-binding protein, which comprises the following steps:

- (a) subjecting the bilin-binding protein to random mutagenesis at at least one of the sequence positions 28, 31, 34, 35, 36, 37, 58, 60, 69, 88, 90, 95, 97, 114, 116, 125, and 127,
- (b) enriching resulting muteins with binding affinity for the digoxigenin group by

selection and isolating said muteins,

(c) subjecting the muteins obtained in step (b) to another random mutagenesis at at least one of the sequence positions 28, 31, 34, 35, 36, and 37, and

(d) again enriching the resulting muteins by selection and isolating of said muteins.

11. (Withdrawn) The method according to claim 10, wherein in step (b) selection is carried out by competitive enrichment.

12. (Withdrawn) The method according to claim 11, wherein free digoxigenin is used for competitive enrichment.

13. (Withdrawn) The method according to claim 10, wherein the enrichment of step (d) is carried out by forming a complex of the muteins with the digoxigenin group and subsequently dissociating the complex.

14. (Withdrawn) The method according to claim 13, wherein the dissociation of the complex of mutein and digoxigenin group is carried out in acidic or basic medium.

15. (Withdrawn - Currently Amended) A method for preparing a mutein ~~or a fusion protein of a mutein~~ of the bilin-binding protein of *Pieris brassicae* ~~according to claim 1~~, said method comprising ~~for preparing a mutein which is obtainable by:~~

(a) subjecting a nucleic acid coding for the a wild type bilin-binding protein (SEQ ID NO: 28) to random mutagenesis at ~~at least one~~ or more of the sequence positions 28, 31, 34, 35, 36, 37, 58, 60, 69, 88, 90, 95, 97, 114, 116, 125, and 127 of the wild type bilin binding protein (SEQ ID NO: 28), thereby obtaining a nucleic acid coding for a mutein of the bilin-binding protein,

(b) enriching resulting mutein with binding affinity for the digoxigenin group by selection and isolating said muteins,

(c) subjecting the muteins obtained in step (b) to another random mutagenesis at ~~at least one~~ or more of the sequence positions, 28, 31, 34, 35, 36, and 37, and,

(d) again enriching the resulting muteins by selection and isolating said muteins,

characterized in that the nucleic acid coding for the mutein ~~or the fusion protein of a~~
~~mutein~~ of the bilin-binding protein is expressed in a bacterial or eukaryotic host cell
and the polypeptide is obtained from the cell or the culture supernatant.

16. [15.] (Withdrawn - Currently Amended) The use of mutein or a fusion protein
of a mutein of the bilin-binding protein according to one or more of claims 1 to 7
of a mutein which is obtainable according to a method according to one or more of
claims 10 to 14 for binding, detecting, determining, immobilizing, or removing
digoxigenin or conjugates of digoxigenin with proteins, nucleic acids, carbohydrates,
other biological or synthetic macromolecules or low molecular weight chemical
compounds.

17. (Withdrawn) A method for detecting the digoxigenin group, wherein a mutein of
the bilin-binding protein or a fusion protein of a mutein of the bilin-binding protein according
to claim 1 or a mutein which is obtainable according to a method which is obtainable by:

(a) subjecting the bilin-binding protein to random mutagenesis at at
least one of the sequence positions 28, 31, 34, 35, 36, 37, 58, 60, 69, 88, 90, 95, 97, 114, 116,
125, and 127,

(b) enriching resulting muteins with binding affinity for the
digoxigenin group by selection and isolating said muteins,

(c) subjecting the muteins obtained in step (b) to another random
mutagenesis at at least one of the sequence positions, 28, 31, 34, 35, 36, and 37, and

(d) again enriching the resulting muteins by selection and isolating
said muteins,

which is brought into contact with digoxigenin or with conjugates of digoxigenin under
conditions suitable for effecting binding of the mutein to the digoxigenin group, and the
mutein or the fusion protein of the mutein is determined.

18. (New) The fusion protein according to claim 6, further comprising a second
fusion partner that is at least one member selected from the group consisting of an
enzyme, a protein, a protein domain, a targeting sequence which allows the transport

of the fusion protein in a specific cell compartment and an affinity peptide and wherein this second fusion partner is fused to the carboxy terminus of the mutein.

19. (New) The fusion protein according to claim 7, further comprising a second fusion partner that is at least one member selected from the group consisting of characterized in that an enzyme, another a protein, or a protein domain, a signal sequence and/or an affinity peptide and wherein this second fusion partner is fused to the amino terminus of the mutein of the bilin binding protein polypeptide.

20. (New) The method of claim 15, wherein the nucleic acid coding for the wild type bilin-binding protein (SEQ ID NO: 28) also codes for a fusion partner, wherein the fusion partner is at least one member selected from the group consisting of an enzyme, a protein, a protein domain, a signal sequence and an affinity peptide and wherein the fusion partner is fused to the amino terminus of the mutein of the bilin binding protein.

21. (New) The method of claim 15, wherein the nucleic acid coding for the wild type bilin-binding protein (SEQ ID NO: 28) also codes for a fusion partner, wherein the fusion partner is at least one member selected from the group consisting of an enzyme, a protein, a protein domain, a targeting sequence which allows the transport of the fusion protein in a specific cell compartment and an affinity peptide and wherein the fusion partner is fused to the carboxy terminus of the mutein of the bilin binding protein.